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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/501,289	06/29/2005	Lone Ronnov-Jessen Petersen	05799.0154USWO	3830

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MERCHANT & GOULD PC
P.O. BOX 2903
MINNEAPOLIS, MN 55402-0903

EXAMINER	
SHEN, WU CHENG WINSTON	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 07/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/501,289	PETERSEN ET AL.	
	Examiner	Art Unit	
	Wu-Cheng Winston Shen	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-31* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-31 are pending in the instant application. Claim 27 is a "use claim" and interpreted as a claim for "A method of using".

Election/Restrictions

2. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions, which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

I. Claim 1-18, drawn to a method for isolating of an at least bi-potent mammary gland tissue cell and an isolated cell derived from luminal epithelial cells of a mammary gland, which is capable of proliferating and differentiating into cells of mammary luminal epithelial and myoepithelial cell linages said isolated cell being capable of forming a cell culture comprising cells which are positive staining for the luminal epithelial marker ESA (ESA+) and negative staining for sialomucin (MUC-), so called (ESA+/MUC-) cells.

II. Claim 19, drawn to a method for testing the toxic effect, if any, of a substance on mammary gland epithelial cells, the method comprising multiple steps including culturing isolated cell being capable of forming a cell culture comprising cells

which are positive staining for the luminal epithelial marker ESA (ESA+) and negative staining for sialomucin (MUC-), so called (ESA+/MUC-) cells.

III. Claims 20-21, drawn to a method for testing the carcinogenic effect, if any, of a substance on mammary gland epithelial cells, the method comprising multiple steps including culturing isolated cell being capable of forming a cell culture comprising cells which are positive staining for the luminal epithelial marker ESA (ESA+) and negative staining for sialomucin (MUC-), so called (ESA+/MUC-) cells.

IV. Claims 22, drawn to a method for testing the ability, if any, of a substance to modulate the differentiation of non-terminal differentiated mammary gland epithelial cells, the method comprising multiple steps including culturing isolated cell being capable of forming a cell culture comprising cells which are positive staining for the luminal epithelial marker ESA (ESA+) and negative staining for sialomucin (MUC-), so called (ESA+/MUC-) cells .

V. Claims 23-24, drawn to a method for screening a substance for its ability, if any, to interact with a cellular protein, the method comprising multiple steps including transfecting isolated cell being capable of forming a cell culture comprising cells which are positive staining for the luminal epithelial marker ESA (ESA+) and negative staining for sialomucin (MUC-), so called (ESA+/MUC-) cells.

VI. Claims 25 and 28, drawn to a method of tissue repair or transplantation in a vertebrate host with an isolated cell being capable of forming a cell culture comprising cells, which are positive staining for the luminal epithelial marker

ESA (ESA+) and negative staining for sialomucin (MUC-), so called (ESA+/MUC-) cells, comprising the step of introducing the cell into the vertebrate host.

VII. Claim 26, drawn to a method of *in vivo* administration of a protein or gene of interest to an individual in need thereof, to prevent and/or treat debilitations, derangements and/or dysfunction and/or other disease states in mammals, comprising the step of administration of a protein of interest to the cell-population being capable of forming a cell culture comprising cells which are positive staining for the luminal epithelial marker ESA (ESA+) and negative staining for sialomucin (MUC-), so called (ESA+/MUC-) cells, and introducing the cells administrated with the protein of interest into said individual.

VIII. Claims 27, 29-30, drawn to a pharmaceutical composition and use of the composition comprising: a therapeutically effective amount of a cell being capable of forming a cell culture comprising cells, which are positive staining for the luminal epithelial marker ESA (ESA+) and negative staining for sialomucin (MUC-), so called (ESA+/MUC-) cells, or cells or tissues derived therefrom; and a pharmaceutically acceptable carrier; and further comprising a proliferation factor or a lineage commitment factor.

IX. Claim 31, drawn to a diagnostic agent comprising the cell being capable of forming a cell culture comprising cells, which are positive staining for the luminal epithelial marker ESA (ESA+) and negative staining for sialomucin (MUC-), so called (ESA+/MUC-) cells, or any part thereof.

Further **restriction** is required for the following claims:

(1). Claims 19, restriction to one response is required: (a) changes in cell growth rate, cell death rate, apotosis, cell metabolism, inter- as well as intra-cellular communication, morphology (b) changes in mRNA expression (c) changes in protein expression (d) changes in antigen expression. Determining different responses will require patentably distinct reagents, steps, and technical considerations.

(2). Claims 20, restriction to one neoplastic response in animals is required: (a) changes in morphology, tumorigenicity (b) changes in mRNA expression (c) changes in protein expression (d) changes in antigen expression. Determining different neoplastic responses will require patentably distinct reagents, steps, and technical considerations.

(3). Claims 21, restriction to a specified immune incompetent test animal is required. Determining test animals will require patentably distinct reagents, steps, and technical considerations for testing the carcinogenic effect.

(4). Claim 22: restriction to one differentiation modulation response is required: (a) changes in cell growth rate, cell death rate, apotosis, cell metabolism, inter- as well as intra-cellular communication, morphology (b) changes in mRNA expression (c) changes in protein expression (d) changes in antigen expression (e) a specific change associated with differentiation. Determining different differentiation modulation responses will require patentably distinct reagents, steps, and technical considerations.

(5). Claim 23: restriction to one interaction with a cellular protein is required: (a) changes in cell growth rate, cell death rate, apotosis, cell metabolism, inter- as well as intra-cellular communication (b) changes in mRNA expression (c) changes in protein expression (d) changes in antigen expression (e) a specific change directly or indirectly associated with the said cellular protein. Determining different interaction with a cellular protein will require patentably distinct reagents, steps, and technical considerations.

(6). Claim 26, restriction to either administration of a protein or administration of a gene to an individual is required. A protein is patentably distinct from a gene (nucleic acid) in term of structure, biochemical and biophysical characteristics, and biological functions. Administration of a protein and a nucleic acid requires patentably distinct reagents, steps, and technical considerations.

(7). Claim 27, restriction to one disease in mammals is required: (a) cellular debilitations, (b) cellular derangements and (c) cellular dysfunctions or (d) a specified disease state. Different diseases require different reagents and steps for treatments and the composition for treatment of one disease cannot be directly applicably to another disease.

It is noted that the abovementioned claims are required for further *restrictions*, **NOT** an *election of species*.

3. The inventions listed as Groups I-IX do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Applicant's claims encompass multiple inventions and do not have a special technical feature which link the inventions one to the other, and lack unity of invention. The common technical feature in all groups, as stated in claim 1, is an isolated cell derived from luminal epithelial cells of a mammary gland, which is capable of proliferating and differentiating into cells of mammary luminal epithelial and myoepithelial cell linages said isolated cell being capable of forming a cell culture comprising cells which are positive staining for the luminal epithelial marker ESA (ESA+) and negative staining for sialomucin (MUC-), so called (ESA+/MUC-) cells. This common technical feature is also reflected in the title of instant application: a suprabasal breast cell with stem cell properties. However, this common technical feature cannot be a special technical feature under PCT Rule 13.2 because the feature is shown in the prior art. In the US Patent 5,650,317 (Chang et al., issued July 22, 1997), Chang et al. teach "human breast epithelial cell type with stem cell and luminal epithelial cell characteristics" (See title and claims 1-4), which is substantially as claimed in claims 1-18 (Group I) of instant application. The reference specially described a method of obtaining the breast epithelial cell type with stem cell and luminal epithelial cell characteristics. It is noted that the expression of markers (ESA+/MUC-), positive staining for the luminal epithelial marker ESA (ESA+) and negative staining for sialomucin (MUC-), was not tested by Chang et al. However, the

expression of these two markers is considered as inherent characteristics of the cells described by Chang et al.

Inventions of the Groups I-IX are patentably distinct each from the other because they are different methods (Groups I-VII), distinct pharmaceutical composition and use thereof (Group VIII), and a diagnostic agent (Group IX). The steps and technical considerations required for the methods of isolating luminal epithelial cell (Group I), testing toxic effect (Group II), testing carcinogenic effect (Group III), testing the ability to modulate differentiation (Group IV), screening for a substance (Group V), tissue repair or transplantation (Group VI), and *in vivo* administration of a protein or a gene (Group VII) are not obvious over each from the other.

The search of the above listed Groups is distinct one from each other and not co-extensive and thereby presents search burdens on the examiner.

4. Because these inventions are independent or distinct for the reasons given above and the inventions require a different field of search (see MPEP § 808.02), restriction for examination purposes as indicated is proper.

5. This application contains claims directed to the following patentably distinct species: a rodent cell, aporcine cell, a ruminant cell, a bovine cell, a caprine cell, a equine cell, a canine cell, a ovine cell, a feline cell and a primate cell. The species listed in claim 13 are independent or distinct because they are cells from distinct sets of mammalian species.

This application also contains claims directed to the following patentably distinct species: cells from mice, cells from rats, and cells from rabbits. The species listed in claim 14 are independent or distinct because they are cells from distinct sets of mammalian species.

This application further contains claims directed to the following patentably distinct species: estrogen receptor-alpha, estrogen-receptor-beta, and progesterone receptor. The species listed in claim 24 are independent or distinct because they are hormone receptors.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, **claim 13, 14, and 24** are generic.

Applicant is advised that a reply to this requirement ***must*** include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

6. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the

currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication from the examiner should be directed to Wu-Cheng Winston Shen whose telephone number is (571) 272-3157 and Fax number is 571-273-3157. The examiner can normally be reached on Monday through Friday from 8:00 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the supervisory patent examiner, Ram Shukla, can be reached on (571) 272-0735. The fax number for TC 1600 is (571) 273-8300. Any inquiry of a general nature, formal matters or relating to the status of this application or proceeding should be directed to Dianiece Jacobs whose telephone number is (571) 272-0532.

Wu-Cheng Winston Shen

RAM R. SHUKLA, PH.D.
SUPERVISORY PATENT EXAMINER

Wu-Cheng Winston Shen, Ph. D.
Patent Examiner
Art Unit 1632